Limited Gene Expression Variation in Human Embryonic Stem Cell and Induced Pluripotent Stem Cell Derived Endothelial Cells.

Journal: Stem Cells

Publication Year: 2012

Authors: Mark P White, Abdul J Rufaihah, Lei Liu, Yohannes T Ghebremariam, Kathryn N Ivey, John P Cooke, Deepak Srivastava

PubMed link: 23079999

Funding Grants: microRNA Regulation of Cardiomyocyte Differentiation from Human Embryonic Stem Cells

Public Summary:
Induced pluripotent stem (iPS) cells have recently emerged as a promising alternative to embryonic stem (ES) cells for modeling disease and developing therapeutics. It is important to explore the differences between these two cell types to pinpoint genetic abnormalities or discover if they have a tendency to differentiate toward a particular cell type. Here, we report an experimental protocol based on embryonic development that produces large numbers of endothelial cells—the cells that line the interior surface of blood vessels—derived from multiple human ES cells or iPS cells. The steps involved in this protocol resulted in an expanding, uniform pool of cells that in all functional aspects were similar to endothelial cells. Comparison of the various kinds of RNA in the cells revealed limited gene expression variability between multiple lines of human iPS–derived endothelial cells, or between lines of ES– and iPS–derived endothelial cells. These results demonstrate a method to generate large numbers of pure human endothelial cell progenitors and differentiated endothelial cells from pluripotent stem cells, and suggest individual lineages derived from human ES and iPS cells may have low variance at the level of gene expression. Given the limited variability, endothelial cells derived from patient-specific iPS cells may prove useful in modeling diseases of the blood vessels or in testing potential new drugs to treat these diseases.

Scientific Abstract:
Recent evidence suggests human embryonic stem (ES) and induced pluripotent stem (iPS) cell lines have differences in their epigenetics marks and transcriptomes, yet the impact of these differences on subsequent terminally differentiated cells is less well understood. Comparison of purified, homogeneous populations of somatic cells derived from multiple independent human iPS and ES lines will be required to address this critical question. Here, we report a differentiation protocol based on embryonic development that consistently yields large numbers of endothelial cells (EC) derived from multiple human ES or iPS cells. Mesoderm differentiation of embryoid bodies was maximized and defined growth factors were used to generate KDR(+) EC progenitors. Magnetic purification of a KDR(+) progenitor subpopulation resulted in an expanding, homogeneous pool of ECs that expressed EC markers and had functional properties of ECs. Comparison of the transcriptomes revealed limited gene expression variability between multiple lines of human iPS--derived ECs, or between lines of ES-- and iPS--derived ECs. These results demonstrate a method to generate large numbers of pure human EC progenitors and differentiated ECs from pluripotent stem cells, and suggest individual lineages derived from human iPS cells may have significantly less variance than their pluripotent founders.